REMARKS

Claims 59-62 and 80-114 are currently pending. Claims 59-62 are withdrawn. Claims 80-114 stand rejected.

Applicants acknowledge that the drawings filed on June 28, 2002 have been accepted by the Examiner.

CLAIMS

Support for amendments made to Claim 85 may be found in the instant specification at page 4, \P [0015]. Claim 115 has been added and is supported throughout the instant specification and by Claim 105.

TITLE

The Examiner has requested a new title that clearly indicates the invention to which the claims are directed. Applicants present herewith a new title.

REJECTIONS UNDER 35 U.S.C. §112

Claims 80-114 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite for the phrase "the first strand cDNA" of claim 80 for lacking proper antecedent basis. The Examiner has further rejected claim 85 for the phrase "a least" which should read "at least." Applicants have amended claims 80 and 85 in order to address the Examiner's concerns. Reconsideration and withdrawal of the 35 U.S.C. §112, second paragraph rejections are respectfully requested.

REJECTIONS UNDER 35 U.S.C. §103

Claims 80-114 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Chenchik, et al. (U.S. 5,962,272) in view of Van Gelder, et al. (U.S. 5,545,522). Applicants respectfully traverse the Examiner's rejection.

There is no motivation or guidance in the cited publications for one skilled in the art to use the claimed synthesis primer and oligonucleotide in the claimed RNA amplification

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method. Further, the examiner has used hindsight to amass the cited art (which does not teach or make obvious applicants' invention) as there is no motivation to combine these particular references in this particular fashion.

The Examiner contends that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to carry out the claimed methods. However, to establish a *prima facie* case of obviousness, three basic criteria must be met [MPEP 2143]. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, (Fed. Cir. 1991).

Applicants submit that claims 80-114 are patentable over Chenchik in view of Van Gelder. Briefly, the Chenchik reference describes a method of preparing a DNA molecule complementary to an RNA molecule using a template switching oligonucleotide for synthesizing and cloning full length cDNA, or cDNA fragments that corresponds to the complete sequence of 5'-mRNA. The Examiner has combined the Chenchik reference with Van Gelder, et al. The Examiner admits that Chenchik does not "explicitly disclose the use of these sequences to form a plurality of RNA transcripts from the synthesized double-stranded cDNA" (Office Action-page 4, ¶3). However, the Examiner contends that it would have been obvious for one of ordinary skill in the art to use "the terminal continuation oligonucleotide and synthesis primer comprising a transcriptional promoter sequence [of Chenchik], to form a plurality of RNA transcripts from double-stranded cDNA because Van Gelder disclosed the advantageous use of such promoter sequences for that purpose" (Office Action- page 5, ¶1). Applicants, however, respectfully traverse that there is any teaching or motivation to combine the method of using the terminal continuation oligonucleotide and synthesis primer comprising a transcriptional promoter sequence of Chenchik and the formation of a plurality of RNA transcripts of Van Gelder in order to result in the claimed invention.

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The Chenchik method involves annealing a cDNA synthesis primer to RNA, and reverse transcribing the cDNA molecule to produce an mRNA-cDNA hybrid. A template switching oligonucleotide hybridizes to the 5′ CAP site and serves as a short, extended template for CAP-dependent extension of the 3′-end of the single-stranded cDNA that is complementary to the template-switching oligonucleotide. The Chenchik method does not, however, provide a plurality of RNA transcripts, but rather generates full length cDNA from RNA forming double-stranded cDNAs for full length cDNA libraries, for example.

Van Gelder reports of synthesizing a cDNA from an RNA primed by a single complementary primer in the reaction, where the primer is linked to the sequence of an RNA polymerase promoter region, and using an RNA polymerase, transcribes amplified antisense RNA from the cDNA. The "need for improved methods of identifying and cloning mRNAs and of accurate in vitro amplification of selected cDNA's...[which the Van Gelder method] fulfills (Col. 2, lns. 18-28) suggests that the Van Gelder method sufficiently fulfills the need in the art without any modification. The Examiner broadly directs the applicants' attention to Van Gelder, Figure 1 and columns 2-10 for support of a transcriptional promoter sequence on a primer for extending a target RNA sequence into a cDNA for advantageously synthesizing a plurality of RNA transcripts using RNA polymerase. Irrespective of the Examiner's contention that "Van Gelder et al. disclosed the advantageous use of such promoter sequences" for forming a plurality of RNA transcripts (Office Action-page 5, ¶1), Van Gelder does not teach or provide guidance for using a synthesis primer and oligonucleotide where one or both comprise a transcriptional promoter sequence of the claimed invention. Furthermore, there is no motivation to modify the Van Gelder primer complex having a primer operably linked to a RNA polymerase promoter region (Figure 1) to obtain the combination of a synthesis primer and oligonucleotide of Chenchik in order to amplify RNA since the Van Gelder primer complex alone is sufficient to amplify RNA. Applicants respectfully request that the Examiner specifically point out in Van Gelder the alleged motivation to combine or modify the Chenchik and Van Gelder methods to result in a method of amplifying RNA using two primers, a terminal continuation oligonucleotide and synthesis primer as claimed in the present invention.

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Therefore, since there is no motivation or suggestion to combine the Chenchik and Van Gelder publications to obtain a method of amplifying RNA using a synthesis primer and terminal continuation oligonucleotide, applicants respectfully request reconsideration and withdrawal of the §103 rejection in view of the above arguments.

CONCLUSION

Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. <u>13-4500</u>, Order No. 1079-4015US3. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. <u>13-4500</u>, Order No. <u>1079-4015US3</u>. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

Respectfully submitted,

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